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EXAMINER	
JEAN-LOUIS, SAMIRA JM	
ART UNIT	PAPER NUMBER
1617	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/525,736	LULLA ET AL.	
	Examiner	Art Unit	
	SAMIRA JEAN-LOUIS	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 February 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9 and 15-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9 and 15-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Arguments

This Office Action is in response to the amendment submitted on 02/13/09. Claims 1-9 and 15-26 are currently pending in the application, with claims 10-14 and 27-33 having being cancelled. Accordingly, claims 1-9 and 15-26 are being examined on the merits herein.

Receipt of the aforementioned amended claims and Attached Study is acknowledged and has been entered.

1. Applicant's argument with respect to the Obviousness Double Patenting (ODP) has been fully considered. Applicant argues that because Meade does not show composition in particulate form having a particle size from nano-size to 12 μm, the ODP is not obvious. Such arguments are not persuasive given that the features upon which applicant relies (i.e., particle size from nano-size to 12 μm) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Consequently, such argument is moot. The Examiner reiterates the fact that co-pending application Lulla '902 teaches a formulation comprising beta-mimetics such as salmeterol and anti-cholinergics such as tiotropium. While Lulla '902 does not teach addition of a corticosteroid, Meade et al. teach the combination of a betamimetic such as salmeterol, anticholinergics such as

tiotropium, in combination with corticosteroids such as fluticasone for the treatment of COPD. Thus, one of ordinary skill in the art would have indeed found it obvious to add corticosteroids in light of the disclosure of Meade et al. who teach the combination of the aforementioned drugs in the treatment of COPD. As to applicant's arguments that in the absence of a steroid, no steroid effect would be seen, such arguments are not persuasive given that the claims are directed to a composition and not to a method of obtaining a steroid-sparing effect. Thus, in light of Meade et al. who teach addition of steroids to the two bronchodilators, a steroid sparing effect would necessarily be present in such a composition. Consequently, the Examiner asserts that the ODP was indeed proper and is therefore maintained.

2. Applicant's argument with respect to the scope of enablement over claims 1-2 has been fully considered. Since applicant has amended the claims, such rejection is now moot. Consequently, the rejection of claims 1-2 under 35 U.S.C. § 112, first paragraph is hereby withdrawn.

3. Applicant's contention that Meade and Keller do not teach the use of particle sizes ranging from nano-size up to 12μm has been fully considered but is not found persuasive. The Examiner respectfully points out that the features upon which applicant relies (i.e., particle size from nano-size to 12 μm) are not recited in the rejected claim(s).

Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Consequently, such argument is moot. As for Applicant's contention that Keller does not exemplify a formulation containing a beta-mimetic, an anticholinergic, and/or a corticosteroid, such argument has again been fully considered but is not found persuasive. The Examiner would like to point out that Keller was used in an obviousness rejection and thus exemplification is not required. Moreover, Keller et al. teach dry powder formulations for inhalation containing active compounds including beta-mimetic such as salmeterol, anticholinergics such as tiotropium, and corticosteroids such as fluticasone. Keller et al. further point out that two or more of the aforementioned compounds can be combined in the dry powder formulations along with carriers. Consequently, one of ordinary skill in the art would have found it obvious to try all three drugs in combination since Keller teaches the combination of two or more drugs. Again, the Examiner reminds applicant that the claims are directed to a composition. Thus, it would have been well within the purview of the skilled artisan to try the combination of salmeterol, tiotropium, and fluticasone since Keller teaches that two or more compounds can be combined. Regardless of the problem being solved by Keller, the fact that Keller discloses the combinatorial use of the aforementioned compounds would have indeed motivated one of ordinary skill in the art to try the trio combination for inhalation. As for applicant's contention that Keller teaches dry powder formulation and thus one of ordinary skill in the art would not have found it obvious to formulate aerosol formulations, the Examiner disagrees. In fact, it is

well known in the art that dry powder formulations can and are known to be formulated in the form of an aerosol. Particularly, Boucher (U.S. 2002/0099023 A1) teaches dry powder aerosol formulation for chronic obstructive airway disease (see abstract). Boucher further teaches that active compounds are deposited on lung airway surfaces by administering an aerosol suspension of solid respirable particles (see pg. 3, paragraphs 0030 and 0033-0034). Thus, in view of the well-known fact of dry powder formulation formulated as aerosol formulations, the Examiner contends that one of ordinary skill in the art would have indeed found it obvious to formulate the composition as a dry powder aerosol formulation if the desire is to deposit the active compound on lung airway surfaces. Finally, in regard to applicant's contention that the triple active combination of the present invention results in a steroid sparing effect and lower reduction in exhaled level of nitric oxide, the Examiner contends that given that the exact same combination is taught by Meade, such product will inherently possess these same characteristics. Consequently, it is the Examiner's contention that Meade anticipates applicant's invention while Keller renders it obvious. Thus, the 102 and 103 rejections of record remain proper and are therefore maintained.

For the foregoing reasons, the 112 first paragraph rejection is withdrawn. The rejections under 35 U.S.C. 102 and 103(a) remain proper and are maintained. However, in view of applicant's amendment, the following modified ODP, 102 (e), and 103 (a) Final rejections are being made.

Provisional Non-Statutory Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In *re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-4, 8, 15-18, 20-22, and 24-25 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3, 5-7, 9-10, and 12-13 of copending Application No. 11/574902 (hereinafter Lulla US Patent Application No. '902) in view of Meade et al. (U.S. 2003/0018019 A1). Although the conflicting claims are not completely identical, they are not patentably distinct from each other because both applications are directed to a formulation comprising beta-mimetics such as salmeterol and anti-cholinergics such as tiotropium administered via inhalation or metered dose inhaler for the treatment of COPD.

While the co-pending application Lulla '902 does not teach addition of corticosteroids, Meade et al. teach the combination of beta-mimetics such as salmeterol and anticholinergics such as tiotropium in combination with corticosteroids such as fluticasone for the treatment of COPD. Consequently, one of ordinary skill would have found it obvious to add corticosteroids to the composition of Lulla '902 since Meade et al. teach their effective combination in the treatment of COPD. Thus, the aforementioned claims of the instant application are substantially overlapping in scope as discussed hereinabove and are prima facie obvious over the cited claims of corresponding application No. 11574902.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-9 and 15-26 are rejected under 35 U.S.C. 102(e) as being anticipated by Meade et al. (2003/0018019 A1, previously cited).

Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

It is respectfully pointed out that a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the limitation of the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See In re Casey, 152 USPQ 235 (CCPA 1967) and In re Otto, 136 USPQ 458, 459 (CCPA 1963). Thus, the intended use for the treatment of conditions is not afforded patentable weight.

Meade et al. teach novel pharmaceutical compositions based on anticholinergics, corticosteroids, and beta-mimetics (see abstract and pg. 1, paragraph 0001). Within the scope of the invention the term anticholinergics 1 denotes salts which are preferably selected from among tiotropium and most preferably tiotropium salts (see pg. 1, paragraph 0004). By salts, the present invention encompasses salts of tiotropium including the bromide salt wherein tiotropium bromide is particularly preferred (instant claims 1-2; see pg. 1, paragraphs 0004-0005). Within the scope of the invention, the word corticosteroids (hereinafter 2) denotes compounds selected from a group which includes fluticasone wherein the most preferred compounds including fluticasone (instant claim 1 and 3; see pg. 1, paragraphs 0006). Any reference to salts of corticosteroids includes sodium salts, propionate salts, etc... (instant claim 2; see pg. 1, paragraph 0007). Examples of beta-mimetics (i.e. 3) which may be used in the present invention include preferred compound salmeterol or its salts including sulfate salts (instant claims 1; see pgs. 1-2, paragraphs 0008-0012). Meade et al. also teach that the three active substances are administered simultaneously in a single active substance formulation or administered successively in separate formulations (instant claim 1-4, 15-16, 20-21, and 24-25; see pg. 1, paragraph 0003). Additionally, Meade et al. teach that beta-mimetics 3 are optionally referred to as beta2-receptor agonists or ß2-agonists (see pg. 2, paragraph 0013). The pharmaceutical combination of 1, 2, and 3 (i.e. salmeterol, tiotropium and fluticasone; applicant's elected species; instant claims 1-4; pg. 3, paragraphs 0023-0025) are preferably administered by inhalation (instant claim 8) and provided in the form of their enantiomers, mixtures of enantiomers or in the

form of racemates, in the form of suitable inhalable powders (instant claims 18 and 22), or inhalation aerosols (instant claim 9, or as a solution (instant claim 23; see pg. 2, paragraphs 0014 and 0020-0022). Additionally, the present invention are administered in a therapeutic effective quantity and administered along with a pharmaceutically acceptable carrier (instant claim 3; see pg. 2, paragraph 0017-0018). The composition can be provided as inhalable powders (instant claim 18) and provided in admixture with excipients such as lactose (instant claims 3 and 19; pg. 5, paragraphs 0032-0035). Moreover, Meade et al. teach that the inhalable powders can be administered by means of metered dose inhalers (instant claim 17; see pg. 6, paragraph 0046 and pg. 7, paragraph 0055), using propellant free inhalable solutions or suspensions of the aforementioned combination (instant claim 23; see pg. 6, paragraphs 0047-0048 and pg. 9, paragraph 0088) or in nebulisers (instant claim 26; see pg. 7, paragraph 0056). Importantly, Meade et al. exemplify the inhalable powder containing tiotropium bromide in an amount of 0.0045% (i.e. anticholinergic %; instant claim 5), fluticasone propionate in an amount of 0.025% (i.e. corticosteroid; instant claim 7), and salmeterol xinafoate in an amount of 0.01% (i.e. B2-agonist; instant claim 6; see pg. 10, paragraphs 0097-0098). Moreover, Meade et al. teach that the micronized active substance 1, 2, and 3 (i.e. anticholinergics, corticosteroids, and beta-mimetics) are preferably with an average particle size of 0.5 to 10 µm (instant claims 1 and 3; see pg. 6, paragraphs 0036 and 0045).

Accordingly the teachings of Meade et al. anticipate claims 1-9 and 15-26.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-9, 15-22, and 24-26 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Keller et al. (U.S. 6,645,466 B1).

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

It is respectfully pointed out that a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the

prior art structure is capable of performing the intended use, then it meets the limitation of the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See In re Casey, 152 USPQ 235 (CCPA 1967) and In re Otto, 136 USPQ 458, 459 (CCPA 1963). Thus, the intended use for the treatment of conditions is not afforded patentable weight.

Keller et al. teach enhanced dry powder formulations for inhalation which contain an ineffective pharmaceutical carrier and a finely divided pharmaceutically active compound of inhalable particle size, i.e. having a mean particle diameter of preferably at most 10 μm(instant claims 1, 3, 8 and 22; see abstract, col. 4, lines 55-67, and col. 9, lines 8-14). According to Keller, the active compounds in the formulation can be various compounds that can be administered by inhalation including a beta-mimetic such as salmeterol, an anti-cholinergic agent such as tiotropium, and a corticosteroid such as fluticasone, or a pharmaceutically acceptable derivative or salt thereof wherein the formulations can contain two or more of the aforementioned active compounds (instant claims 1, 3, 15, 20-21, and 24; see col. 6, lines 1-3 and 13-37). Additionally, Keller et al. teach the use of carriers such as lactose in multi-dose dry powder inhalers for improved flow properties and lubricating properties (see col. 3, lines 47-67). Salts or esters of the pharmaceutical compounds can be provided in the form a of salt including bromide, sulfate, propionate, etc...(instant claims 2, 4, 16, and 25; see col. 6, lines 40-50). Additionally, Keller et al. teach the use of magnesium stearate if the formulation contains a beta-mimetic such as salmeterol, and an anti-cholinergic such as tiotropium bromide, and a corticosteroid such as fluticasone bromide (see col., lines 52-66).

Additionally, the active compound can range approximately from 0.1%-10% by weight (instant claims 5-7; see col. 7, lines 11-22). All customary carriers used in dry powder inhalation can be used including mono and di-saccharides such as lactose (see col. 8, lines 1-4) and administered in a multi dose dry powder inhaler (col. 9, lines 21-27).

Keller et al. do not exemplify a formulation containing a beta-mimetic, an anti-cholinergic, and a corticosteroid. Similarly, Keller et al. do not teach the composition as an aerosol, in a nebuliser or a metered-dose inhaler.

Keller et al., however do teach that the formulations can contain two or more pharmaceutically active compounds (see col. 6, lines 13-37). Keller et al. further teach the use of magnesium stearate in dry powder formulations which contain a beta-mimetic, and/or an anti-cholinergic, and/or a corticosteroid or formulations in the form of the compounds' pharmaceutical salts such as salmeterol xinafoate, tiotropium bromide, and fluticasone propionate (applicant's elected species; see col. 6, lines 57-65).

Thus, to one of ordinary skill in the art at the time of the invention would have found it obvious to combine the active compounds disclosed by Keller et al. into a formulation since Keller et al. teach their use in dry powder formulations. Likewise, one of ordinary skill in the art at the time of the invention was made would have found it obvious to formulate the composition as an aerosol, in a nebuliser or a metered dose inhaler for proper delivery of the composition and given that it is well known in the art to

formulate dry powder formulations as aerosols, in nebulizers or in metered dose inhalers. Moreover, one of ordinary skill would have found it obvious to substitute fluticasone for its salts (i.e. fluticasone propionate) given that the substitution of one known element for another would have yielded predictable results.

Thus, given the teachings of Keller et al., one of ordinary skill would have been motivated to combine the beta-mimetic agent disclosed by Keller et al. with the anti-cholinergic agent, along with the corticosteroid and formulate the preparation in different forms since Keller et al. teach their use in dry powder inhalers for improved moisture resistance with the reasonable expectation of providing a formulation that is effective in moisture resistance.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samira Jean-Louis whose telephone number is 571-270-3503. The examiner can normally be reached on 7:30-6 PM EST M-Th.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/S. J. L. /

Examiner, Art Unit 1617

04/29/2009

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1617